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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HARRIS, ALANA M	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 10/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/809,638	FARIS ET AL.	
	Examiner	Art Unit	
	Alana M. Harris, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 July 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,7,14 and 23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7,14 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *18* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Response to Amendment and Arguments

1. Claims 1, 7, 14 and 23 are pending.

Claims 2, 3 and 8 have been cancelled.

Claims 2, 7, 14 and 23 have been amended.

Claims 1, 7, 14 and 23 are examined on the merits.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Drawings

3. The drawings submitted July 14, 2003 as Paper number 20 have been accepted by the draftsman.

Withdrawn Objections

Specification

4. The disclosure is no longer objected to because Applicants have amended the specification to include essential information and embedded hyperlinks and/or other form of browser-executable code have been deleted.

Claim Objections

5. The objection of claims 2-4 under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim is withdrawn in light of the claim amendments.

Withdrawn Rejection

Claim Rejections - 35 USC § 112

6. The rejection of claims 1-4, 7, 14 and 23 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is withdrawn. Claim 8 has been cancelled.

7. The rejection of claims 1-4, 7, 14 and 23 under 35 U.S.C. 112, first paragraph, because the specification, does not reasonably provide enablement commensurate with the scope of the claimed invention is withdrawn. Claim 8 has been cancelled.

Claim Rejections - 35 USC § 101

8. The rejection of claims 1-4, 7, 14 and 23 under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, credible or substantial asserted utility or a well established utility is withdrawn in view of Applicants' arguments and submitted Exhibits. Claim 8 has been cancelled.

Maintained and New Grounds of Rejection

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 7 and 23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **THIS IS A NEW MATTER REJECTION.** Applicants have amended the claims to recite "at least 90% identical to the entire amino acid sequence of SEQ ID NO: 2, wherein any substitutions are conservation substitutions and binds to an antibody raised by immunization with a protein of SE ID NO: 2, that is immunospecific thereof". Applicants have not pointedly expressed where in the specification support can be found for the newly added phrase. Applicants are requested to provide the page and line numbers with in the disclosure that support the recitation or deleted the new matter.

11. Claims 1-4, 7, 14 and 23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as

to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In anticipation of the instant rejection Applicants aver that as amended the claims no longer are directed to a 125P5C8-related protein and the claims have functional language. Applicants further assert "...that they are entitled to a reasonable scope of protection" and Example 14 of the Written Description Guidelines support the amended claim language and accordingly the instant rejection should not be applied. These points of view have been carefully considered, but found unpersuasive.

Claim 1 is broadly drawn to "[an] isolated 125P5C8 protein comprising the sequence of SEQ ID NO: 2". Claims 7 and 23 are broadly drawn to an isolated 125P5C8 protein that is at least 90% identical to SEQ ID NO: 2, has at least 6-30 contiguous amino acids of SEQ ID NO: 2 and conservative substitutions, as well as capable of binding to an antibody raised by immunization with a protein of SEQ ID NO: 2. The written description in this instant case only sets forth polypeptide, SEQ ID NO:2. The specification has defined 125P5C8 proteins which encompasses variants, homologs or analog polypeptides, see page 19, lines 27-29. The written description is not commensurate in scope with the claims drawn to 125P5C8 polypeptides that are 90% identical to SEQ ID NO: 2, as well as variant and mutated polypeptides.

Claim language setting forth that the protein binds to an antibody raised by immunization with a protein of SEQ ID NO: 2 does not aid Applicants in obviating this instant rejection. The antibody that binds with a protein does not establish that protein's function, nor aid in establishing the protein's intrinsic activity. By no means does the

binding of an antibody to a protein define the function or the structure of the said protein. The antibody limitation within the claims does not provide any indication of the function of SEQ ID NO: 2. And in regards to Example 14 the intrinsic functional activity of the claimed protein is defined. Applicants' claims are not commensurate to the Example provided in the Written Description Guidelines. Accordingly, the instant rejection is set forth.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 115).

With the exception of SEQ ID NO:2, the skilled artisan cannot envision the detailed structure of the encompassed polypeptides and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The polypeptide itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Furthermore, In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

At the time the application was filed Applicants only had possession of SEQ ID NO: 2 and not polypeptides that share less than 100% sequence identity with SEQ ID NO:2. The specification does not evidence the possession of all the possible mutant polypeptides that could be capable exhibiting the alleged wild type 125P5C8 properties listed on pages 10-13, such as a diagnostic marker. There is insufficient to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

The full breadth of the claims do not meet the written description provision of 35 U.S.C. 112, first paragraph.

12. Claims 1-4, 7, 14 and 23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, does not reasonably provide enablement commensurate with

the scope of the claimed invention. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Applicants head the arguments to the previous enablement rejection as "Written Description" on page 12 of the remarks. The rejection on pages 6-11, paragraph 9 set forth in the first action on the merits (mailed March 27, 2003) was not a 112, first paragraph based on lack of written description, but based on lack of enablement. Applicants assert that the Office acknowledges that SEQ ID NO: 1 and SEQ ID NO: 2 are enabled and "the present claims include a genus of proteins that have substantial homology to SEQ ID NO: 2, and have the functional property of ...SEQ ID NO: 2". These arguments have been carefully considered, but are found unpersuasive.

Applicants are not enabled for a 125P5C8 protein, which is SEQ ID NO: 2 and the polynucleotide sequence of SEQ ID NO: 1, nor variants, homologs or analog polypeptides encompassed by the term, 125P5C8. As stated in the written description rejection above the specification has defined 125P5C8 proteins which encompasses variants, homologs or analog polypeptides, see page 19, lines 27-29. Furthermore, the claims continue to embody proteins with conservative substitutions and proteins with at least 90% identity to SEQ ID NO: 2. Accordingly, the claims are still rejected. The specification asserts that the instant specification describes a novel gene, designated as 125P5C8, which is over-expressed in a multiple cancers (prostate, bladder, kidney and colon), see page 2, lines 14 and 15; Table 1 on page 73. The specification has insufficient evidence supporting the enablement for the 125P5C8 polypeptides having

the amino acid sequence of SEQ ID NO: 2, variants encompassed by the acronym and polypeptides have less 100% sequence identity with undefined conservative substitutions. The variants encompass allelic variants, conservative substitution variants, analogs and homologs. The specification does not provide for a method of making 125P5C8 proteins based on fragment polynucleotides and polypeptides 90% identical to 125P5C8. Applicants have suggested art-accepted means within the specification by which modifications of 125P5C8 polynucleotides and polypeptides may be produced, see pages 20-22. However, the specification has yet to evidence that any 125P5C8 products (SEQ ID NO: 2, variants, mutants thereof and 90% sequence identical protein thereof) manufactured by these modifications possess functions that are commensurate with the functions of the native protein The less than 100% sequence identical amino acids and sequence identical nucleic acids encoding variant proteins may not maintain the activities proposed in the specification. It would seem that specific function(s) would be required to make the encoded protein useful for the applications disclosed in the specification, such as for treating disorders related to prostate, bladder, kidney and colon cancer, see Table 1, page 72 and providing immunogenic or therapeutic compositions and strategies for treating cancers that express 125P5C8. Since the amino acid sequence of a polypeptide determines its structural and functional properties, predictability of which changes can be tolerated in a polypeptide's amino acid sequence and still retain similar activity requires a knowledge of and guidance with regard to which amino acid or acids in the polypeptide's sequence, if any, are tolerant of modification and which are conserved and detailed knowledge of

the ways in which the protein's structure relates to its function. The specification provides essentially no guidance as to which of the infinite possible choices is likely to be successful. The true fact of the state of the art in peptide chemistry is expressed succinctly in the accompanying Lazar article (Molecular and Cellular Biology 8(3): 1247-1252, March 1988). This article presents data that substantiates the fact that the introduction of mutations in an amino acid sequence will yield products with different biological activity from the wild type protein.

From the discussion above, it is clear that the predictability of changes to the amino acid sequence is practically nil as far as biological activities are concerned. The specification fails to provide sufficient guidance to enable one of ordinary skill in the art to make and use the claimed nucleic acids in a manner reasonably correlated with the broad scope of the claims. Without sufficient guidance, the changes which must be made in the nucleic acid sequence, SEQ ID NO: 1 and amino acid residues of SEQ ID NO: 2, which results in less than 100% sequence identity is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue.

Likewise, Applicants have not provided any disclosure enabling the use of 125P5C8 proteins (SEQ ID NO: 1, SEQ ID NO: 2, variants and 90% sequence identical proteins, thereof) for therapeutics or as a diagnostic marker for a specific type of cancer. There is no disclosure designating what variations of SEQ ID NO: 2 could be regarded as enabling one of ordinary skill in the art to use the sequences in any diagnostic method. The experimental design presented in the specification lacks information

regarding the applicability of SEQ ID NO: 2 and bound sections of the sequences in diagnostic methods relative to any type of cancer. Given the differing hybridization patterns presented in Figure 5 it is not reasonable to conclude that any sequence regarded as a 125P5C8 protein and nucleic acid encoding the protein would be effective in yielding a discriminate diagnosis between distinct disorders, particularly prostate cancer. Tockman et al. (Cancer Research 52:2711s-2718s, 1992) teach considerations necessary for a suspected cancer biomarker (intermediate end point marker) to have efficacy and success in a clinical application. Although the reference is drawn to biomarkers for early lung cancer detection, the basic principles taught are clearly applicable to other oncogenic disorders. Tockman teaches that prior to the successful application of newly described markers, research must validate the markers against acknowledged disease end points, establish quantitative criteria for marker presence/absence and confirm marker predictive value in prospective population trials, see abstract. Early stage markers of carcinogenesis have clear biological plausibility as markers of preclinical cancer and **if validated** (emphasis added) can be used for population screening (p. 2713s, column 1). The reference further teaches that once selected, the sensitivity and specificity of the biomarker must be validated to a known (histology/cytology-confirmed) cancer outcome. The essential element of the validation of an early detection marker is the ability to test the marker on clinical material obtained from subjects monitored in advance of clinical cancer and *link* those marker results with subsequent histological confirmation of disease. "This irrefutable link between antecedent marker and subsequent acknowledged disease is the essence of a valid

intermediate end point [marker]", see page 2714s, column 1, Biomarker Validation against Acknowledged Disease End Points section. Clearly, prior to the successful application of newly described markers, markers must be validated against acknowledged disease end points and the marker predictive value must be confirmed in prospective population trials, see page 2716s, column 2, Summary section. Tockman reiterates that the predictability of the art in regards to cancer prognosis and the estimation of life expectancies within a population with a disease or disorder is highly speculative and unpredictable.

Based on the analysis and the teachings presented above it would require undue experimentation for the skilled artisan to practice this invention because there is no support in the specification for the enablement of the broadly claimed invention. Therefore, in view of the insufficient guidance in the specification, extensive experimentation would be required to enable the claims and to practice the invention as claimed.

13. The rejection of claim 14 under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing to provide an enabling disclosure without complete evidence either that the claimed biological materials are known and readily available to the public or complete evidence of the deposit of the biological materials is maintained for the reasons of record and stated below.

Applicants aver that the deposit of PTA-3137 was made under the terms of the Budapest Treaty and that all restrictions were met. This argument has been found

unpersuasive. The disclosure is still remiss of any documentation supporting the deposit and the stipulations that must be met. The first action on the merits set forth the requirements that must be met by Applicants, specifically stating that the assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit. Applicant's attention is directed to In re Lundak, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR 1.801-1.809 for further information concerning deposit practice.

14. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claims 2-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 2-4 are vague and indefinite. Independent claim 2 recites "consisting of the sequence of SEQ ID NO: 2, wherein the 125P5C8 protein has at least 6[, 15 or 30] contiguous amino acids of ...[the said sequence]". Inherently, the a sequence consisting of SEQ ID NO: 2 would have contiguous amino acids of at least 6-30 amino acids residues. The limitation that the protein must have at least the specified number of amino acid residues is superfluous.

Claim Rejections - 35 USC § 102

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

17. Claims 2-4, 7, 14 and 23 are rejected under 35 U.S.C. 102(a) as being anticipated by Accession number Q9H720 (March 1, 2001), as evidenced by Accession number AK025164 (September 29, 2000). The preamble for claim 14 contains open or comprising language which does not limit the anticipatory protein to a full-length protein, thereby the Examiner is applying the following rejection. Accession #Q9H720 discloses a 125P5C8 protein consisting of the sequence of SEQ ID NO: 2, wherein the disclosed protein has at least 30 contiguous amino acids. The disclosed protein is at least 90% identical to the entire amino acid sequence of SEQ ID NO: 2 and would clearly bind to an antibody raised by immunization with a protein of SEQ ID NO: 2. The disclosed amino acid sequence is encoded by a polynucleotide consisting of the sequence as shown in SEQ ID NO: 1 from nucleotide residue number 82 through nucleotide residue number 696, which is the same as accession number AK025164 nucleic acid residues 264 through 878. This accession number also discloses a protein which has an amino acid sequence which is that of an amino acid sequence encoded by a polynucleotide of at least 10 bases that comprises the base at positions 339, 1119 and 2065, see attached database sheets.

18. Claims 2-4, 7, 14 and 23 are rejected under 35 U.S.C. 102(a) as being anticipated by Accession number AK025164 (September 29, 2000). The preamble for claim 14 contains open or comprising language which does not limit the anticipatory protein to a full length protein, thereby the Examiner is applying the following rejection. Accession #AK025164 discloses a 125P5C8 protein which is at least 90% identical to SEQ ID NO: 2 and has an amino acid sequence encoded by a polynucleotide consisting of the sequence as shown in SEQ ID NO: 1 from nucleotide residue number 82 through nucleotide residue number 696, which is the same as accession number AK025164 nucleic acid residues 264 through 878. This accession number also discloses a protein which has an amino acid sequence which is that of an amino acid sequence encoded by a polynucleotide of at least 10 bases that comprises the base at positions 339, 1119 and 2065, see attached database sheets.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (703) 306-5880. The examiner can normally be reached on 7:00 am to 4:30 pm, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached on (703) 308-3995. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703)308-0196.

ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER

Alana M. Harris, Ph.D.
1 October 2003